DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
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October 30, 2015

ACCUMETRICS, INC.
FRANK LADUCA
CHIEF SCIENTIFIC OFFICER
3985 SORRENTO VALLEY BLVD.
SUITE B
SAN DIEGO, CA92121

Re: K141427
Trade/Device Name: VerifyNow PRUTest
Regulation Number: 21 CFR 684.5700
Regulation Name: Automated platelet aggregation system
Regulatory Class: Class II
Product Code: JOZ
Dated: July 23, 2015
Received: July 24, 2015

Dear Dr. LaDuca:

This letter corrects our substantially equivalent letter of July 24, 2015.

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Leonthena R. Carrington -S

Leonthena R. Carrington, MS, MBA, MT (ASCP)
Director
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Center for Devices and
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Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K141427

Device Name
VerifyNow PRUTest

Indications for Use *(Describe)*
The VerifyNow PRUTest is a whole blood test used in the laboratory or point of care setting to measure the level of platelet P2Y12 receptor blockade. For in vitro diagnostic use. For professional use only.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) Summary

This 510(k) summary is submitted in accordance with 21 CFR §807.92.

Owner: Accumetrics, Inc.
3985 Sorrento Valley Blvd.
San Diego, CA 92121 USA
Contact: Frank M. LaDuca, PhD; Chief Scientific Officer
Telephone: (858) 263-2450
Fax: (858) 875-0603

Prepared: 22 July 2015

Trade name: Accumetrics, Inc. VerifyNow PRUTest ™

Common name: Platelet reactivity test

Classification name: Automated platelet aggregation system
(21 CFR §864.5700; Product Code: JOZ)

Predicate device: VerifyNow P2Y12 Assay, Accumetrics, Inc., k051231

Device description:

The VerifyNow System is a turbidimetric-based optical detection system that measures platelet-induced aggregation. The system consists of an instrument, a disposable test device and quality control materials. Quality control measures include an instrument based electronic quality control (EQC), two levels of wet quality controls (WQC), internal quality controls, and shipping controls. The instrument controls all assay sequencing, temperature, reagent-sample mixing and performs self-diagnostics. The degree of platelet function is determined and the result is displayed.

The VerifyNow PRUTest device contains three lyophilized reagent pellets in separate reaction chambers within the test device: 1) ADP pellet consisting of a preparation of Fibrinogen and BSA coated beads, adenosine-5-diphosphate (ADP), prostaglandin E1 (PGE1), dye, buffer, and a preservative; 2) TRAP pellet (Internal Control) consisting of a preparation of iso-TRAP (Thrombin Receptor Activating Peptide), Fibrinogen and BSA coated beads, buffer, dye, and a preservative; and 3) No-Agonist Pellet (NAP) consisting of a preparation of BSA coated beads, dye, buffer, and a preservative.

Test principle:

The patient sample is citrate-anticoagulated whole blood, which is automatically dispensed from the blood collection tube into the test device by the instrument, with no blood handling required by the user. Fibrinogen-coated microparticles are used in the VerifyNow PRUTest device to bind activated platelet GP IIb/IIIa receptors. ADP is incorporated into the assay to activate platelets, and the reagent is formulated to specifically measure P2Y12-mediated platelet aggregation.

When the activated platelets are exposed to the fibrinogen-coated microparticles, aggregation occurs in proportion to the number of activated platelet receptors. The VerifyNow PRUTest reports results in P2Y12 Reaction Units (PRU).

Intended use:

The VerifyNow PRUTest is a whole blood test used in the laboratory or point of care setting to measure the level of platelet P2Y12 receptor blockade. For *in vitro* diagnostic use. For professional use only.

Indications for use:

Same as the intended use.

Summary of the technological characteristics of the VerifyNow PRUTest (subject device) compared to VerifyNow P2Y12 Assay (predicate device):

The technological characteristics of the Accumetrics Inc. VerifyNow PRUTest are compared with the VerifyNow P2Y12 Assay (k051231) in the table below. This comparison demonstrates the substantial equivalence of this device to the predicate device. The devices are similar in intended use, principle of operation and specimen type. Both devices have similar analytical performance. The modifications from the predicate device are:

Reagents:

- ADP pellet: The reagent pellet was reformulated to contain 80% Fibrinogen/20% BSA coated beads from the previous 100% Fibrinogen coated beads.
- TRAP pellet: This reagent was moved from channel 4 to channel 3. The formulation was unchanged. This channel is used as an internal assay control.
- NAP pellet: The No-Agonist pellet was introduced to channel 4. The purpose of this channel is to prevent a software error and provide no further input into the algorithm for generating the PRU result.

Controls (WQC):

- Level 1 (B-Carbon Sol Filler): This control was reformulated to contain BSA instead of Fish Skin Gelatin.
- Level 2: The GPRP peptide conjugate length was modified from 2 x 10^6 MW AD to 500 MW AD.

Test Device/Instrumentation:

- The humidity sensor was removed from the test device.
- Port cover added to instrument.
- The instrument reports results for the ADP pellet measurement in PRU units.

Table A. Comparison of Predicate to Subject Device

Item	Accumetrics, Inc. VerifyNow PRUTest (Subject Device)	Accumetrics, Inc. VerifyNow P2Y12 Assay (k051231) (Predicate Device)
Similarities		
Principle of Operation	Fibrinogen bead / platelet aggregation with optical detection.	Same.
Specimen Type	Citrate-anticoagulated whole blood.	Same.
Testing Site	Point of care or laboratory.	Same.
Assay Results	P2Y12 Reaction Units (PRU).	Same.
Controls	Pre-packaged, two-level Wet Quality Controls (WQC); Internal control in each assay device.	Same.
Test Procedure	1. Add cartridge to instrument. 2. Attach blood collection tube. No other operator intervention.	Same.
Calibration	Factory.	Same.
Time to result	3 minutes.	Same.
Analytical Claims	Hematocrit range = 33-52%	Same.
Modifications		
Intended Use	The Accumetrics, Inc. VerifyNow PRUTest is a whole blood test used in the laboratory or point of care setting to measure the level of platelet P2Y12 receptor blockade. For *in vitro* diagnostic use. For professional use only.	The VerifyNow P2Y12 Assay is a whole blood assay used in the laboratory or point of care setting to measure the level of platelet $P2Y_{12}$ receptor blockade.
Reagents	ADP Pellet contains 80% Fibrinogen/20% BSA coated beads	ADP Pellet contains 100% Fibrinogen coated beads
	TRAP Pellet found in channel 3.	TRAP Pellet found in channel 4.
	NAP Pellet introduced into channel 4.	No NAP Pellet
Controls	Level 1 (B-Carbon Sol Filler) contains BSA	Level 1 (F-Carbon Filler) contains Fish Skin Gelatin
	Level 2 GPRP Peptide Conjugate length truncated to 500,000 kDa	Level 2 GPRP
Test Device	No humidity sensor	Contains humidity sensor
Analytical Claims	Stability = 9 months (ongoing real-time study in process)	Stability = 18 months

Reference range:

A reference range study (Healthy Donor PRU Reference Range) was conducted to measure platelet function in a healthy donor population using VerifyNow PRUTest. A total of 152 evaluable healthy donors were recruited and their blood samples tested with the VerifyNow PRUTest. The data were evaluated as recommended in EP28-A3c *"Defining, Establishing and*

Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline – Third Edition." The reference range determined from this study, expressed as the central 95% Confidence Interval of the mean, is 182–335 PRU. The data are summarized in the table below.

Table B. Reference Range

			95% confidence interval (CI)	
N	**Mean**	**SD**	**Lower limit (95% CI)**	**Upper limit (95% CI)**
152	266	42	182 (116–197)	335 (324–354)

Expected PRUTest values:

Treatment-naïve patients in the intended use population

Whole blood samples from 84 patients with acute coronary syndrome (ACS) that were not receiving a P2Y12 receptor inhibiting drug were tested with VerifyNow PRUTest. The data were evaluated as recommended in EP28-A3c *"Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline – Third Edition."* The range of values expressed as the central 95% Confidence Interval of the mean is 180–376 PRU. The data are summarized in the table below.

Table C. Expected PRU values in treatment-naïve patients

			95% confidence interval (CI)	
N	**Mean (PRU)**	**SD (PRU)**	**Lower limit (95% CI)**	**Upper limit (95% CI)**
84	274	48	180 (160–200)	376 (358–395)

ACS patients receiving treatment with clopidogrel

Whole blood samples from 71 patients with ACS receiving dual treatment with aspirin and clopidogrel were tested with VerifyNow PRUTest. The data were evaluated as recommended in EP28-A3c *"Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline – Third Edition."* The range of values expressed as the central 95% Confidence Interval of the mean is 6–300 PRU. The data are shown in the table below.

Table D. Expected PRU values in patients receiving clopidogrel treatment

			95% confidence interval (CI)	
N	**Mean (PRU)**	**SD (PRU)**	**Lower limit (95% CI)**	**Upper limit (95% CI)**
71	156	73	6 (0–34)	300 (269–329)

Performance studies

Method Comparison

A method comparison study (VerifyNow P2Y12 and PRUTest Method Comparison Study) was performed using the VerifyNow P2Y12 Assay System (predicate device) and the VerifyNow PRUTest System (subject device). A total of three investigational intended use sites were used to gather data for this investigation. The VerifyNow test analysis was performed at each site by intended users who were trained by the manufacturer. Test device and instrument configurations are described below.

Results:

The PRU results from both the VerifyNow P2Y12 (predicate device) and VerifyNow PRUTest (subject device) demonstrate comparable performance, with a slope not statistically significantly different from 1.0 and an intercept not statistically significantly different from 0, and a correlation (r) greater than 0.9 as shown in the table below.

Table E. Method Comparison

Comparison	N	Regression Method	Slope (95% CI)	Slope p-value	Intercept (95% CI)	Correlation Coefficient R
P2Y12 Rep 1 vs. PRUTest Rep 1	119	Ordinary Least Squares	1.01 (0.97–1.05)	0.56	-0.77 (-8.00–6.50)	0.98
P2Y12 Avg. vs. PRUTest Avg.	119	Ordinary Deming	1.04 (1.00–1.07)	0.07	-4.57 (-11.2–2.05)	0.98

CLSI Precision Studies

Complex precision for the VerifyNow PRUTest was assessed using Wet Quality Controls (WQC), Levels 1 and 2, and intermediate precision was assessed using whole blood samples from healthy donors and from ACS patients receiving clopidogrel with or without aspirin by testing three different lots of test devices and three instruments. Data were analyzed in accordance with Clinical Laboratory Standards Institute (CLSI) guidance EP05-A2, "*Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline – Second Edition.*"

Testing over several days with samples from the same patient is expected to yield variable results between days because platelet reactivity in response to orally ingested medications known to vary based upon time between dosages, as well as the time between dosage and blood collection. A summary of the precision verification studies performed is shown in Table F.

Table F. Description of precision studies

Type	Description
Complex precision using WQC Levels 1 and 2	Measured intermediate precision with WQC Level 2 samples over multiple days.
Complex precision between instruments using WQC Level 2	Measured Level 2 WQC between-instrument precision over multiple days using a single lot of PRUTest devices.
Intermediate precision using whole blood samples from donors and ACS patients	Measured intermediate precision and instrument-to-instrument precision with whole blood samples over multiple days using subjects on dual antiplatelet therapy, healthy subjects dosed *in vivo* with P2Y12 clopidogrel / P2Y12 inhibitor, and normal healthy donors
Intermediate precision between instruments using whole blood samples from donors and ACS patients	Measured whole blood between-instrument precision over multiple days using a single lot of PRUTest devices.

Complex precision using WQC Levels 1 and 2:

WQC Level 1 and Level 2 samples were tested over 20 nonconsecutive days. WQC Level 1 is a negative control (blank) from which no aggregation is expected. All WQC Level 1 results fell within the acceptable range of ≤ 30 PRU and data are not shown. WQC Level 2 results are detailed below. Analysis of variance (ANOVA) was used to estimate the components of variance in accordance with CLSI guidance EP05-A2.

Table G. Reproducibility using WQC Level 2

Between-lot

	Mean	Within-run		Between-run		Between-day		Between-lot		Total	
N	PRU	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
240	300.5	13.6	4.5	7.7	2.5	8.3	2.8	13.5	4.5	22.2	7.4

Between instrument

	Mean	Within-run		Between-run		Between-day		Between-lot		Total	
N	PRU	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
240	302.7	22.6	7.5	0.0	0.0	8.5	2.8	0.0	0.0	24.2	8.0

Intermediate precision using whole blood samples

Whole blood samples from nine donors were drawn once or twice a day, run in duplicate, using three device lots on three instruments over a minimum of five non-consecutive days. Analysis of variance (ANOVA) was used to estimate the components of variance within individual donors in accordance with CLSI guidance EP05-A2. The results of these precision measurements are

detailed in the following two tables. Table H evaluates precision across multiple PRUTest device lots using whole blood samples. Table I evaluates precision across multiple VerifyNow instruments using whole blood samples.

Table H: Precision of whole blood samples – multiple lot experiment

					Mean	Within-run		Between-run		Between-day		Between-lot	
ID	**Rx[1]**	**Days**	**Runs**	**Reps**	**PRU**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
				Acceptance criteria:			**<10**		**<10**		**N/A[2]**		**<10**
1	2	5	1	30	64	4.7	7.4	---	---	9.6	15.0	0.0[3]	0.0[3]
2	0	10	2	118	244	10.4	4.2	0.0	0.0	21.9	9.0	0.0	0.0
3	1	5	2	60	162	6.3	3.9	5.1	3.1	17.7	10.9	0.0	0.0
4	1	5	2	30	190	12.0	6.3	---	---	15.1	7.9	0.0	0.0
5	0	10	2	120	289	11.2	3.9	7.7	2.7	27.0	9.3	0.0	0.0
6	2	5	1	30	221	8.9	4.0	---	---	17.0	7.7	0.0	0.0
7	1	8	2	96	123	9.6	7.8	18.7	15.1	57.6	46.7	0.0	0.0
8	1	10	2	114	216	13.0	6.0	7.3	3.4	16.5	7.6	0.0	0.0
9	2	5	1	30	163	10.9	6.7	---	---	13.3	8.2	0.0	0.0

Table I: Precision of whole blood samples – multiple instrument experiment

					Mean	Within-run		Between-run		Between-day		Between-lot	
ID	**Rx[1]**	**Days**	**Runs**	**Reps**	**PRU**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
				Acceptance criteria:			**<10**		**<10**		**N/A[2]**		**<10**
1	2	5	1	30	67	7.3	10.8	---	---	9.3	13.8	0.0[3]	0.0[3]
2	0	8	2	89	253	13.6	5.4	0.0	0.0	20.4	8.1	9.3	3.7
3	1	5	2	60	160	9.3	5.8	4.1	2.5	18.1	11.3	3.6	2.3
4[4]	1	0	0	0	---	---	---	---	---	---	---	---	---
5	0	9	2	101	290	10.7	3.7	5.4	1.9	21.4	7.4	11.4	3.9
6	2	5	1	30	229	7.9	3.5	---	---	14.4	6.3	8.1	3.5
7	1	5	2	60	115	8.8	7.6	20.4	17.7	65.9	57.1	0.0	0.0
8	1	5	2	54	231	14.7	6.4	12.1	5.3	9.2	4.0	7.9	3.4
9	2	5	1	30	160	11.2	7.0	---	---	11.6	7.3	0.0	0.0

Key: [1] 0 = healthy, no treatment; 1 = dual therapy with clopidogrel plus aspirin; 2 = healthy, given clopidogrel 75 mg/day; [2] not applicable as acceptance criteria for this parameter is undefined as explained in the text; [3] between-lot SD of 0 and %CV of 0 can be observed when the contribution of one source of variability is very small relative to other sources of variability, or if all of the sample elements are the same; [4] Donor 4 had insufficient blood volume to allow for inclusion in the multiple instrument experiment

Open Pouch Device Stability

Extended Open Pouch Stability at Elevated Humidity was conducted to evaluate the stability of the reagents in the PRUTest test device when exposed to environmental humidity. The results of the study are detailed below.

Table J. Open Pouch Device Stability

Time unpouched	PRU whole blood Mean (n=3)	Pct. recovery	PRU WQC Level 2 Allowable range 230–362
0	274	100.0	286
10	277	101.1	254
14	Attention 32*	N/A	3
18	Attention 32*	N/A	7
22	Attention 32*	N/A	18
26	Attention 32*	N/A	21

*Attention 32 is generated because the initial DC value is too high, and the VerifyNow system recognizes that either the blood sample and reagent is too clear, or the reagent pellet is not performing as intended

Percent recovery of VerifyNow PRUTest values in whole blood met the acceptance criteria after exposure to 61-73% RH and 21-24°C temperatures for 10 hours. PRU result with WQC Level 2 remained within the allowable range for 10 hours under the same conditions. These findings support a claim of 10 hour open-pouch stability.

Sample Wait Time and Sample Stability

A sample stability and sample wait time study was conducted to determine the appropriate values. Sample wait time was determined to be 10 minutes, meaning that a blood sample must be stored for a minimum of 10 min after collection by venipuncture. Sample stability was determined to be four hours, meaning that the blood sample must be assayed prior to four hours from the time of blood draw.

Interfering substances

An "interference screen," was performed which followed the recommendations outlined in Clinical Laboratory Standards Institute (CLSI) guidance *EP07-A2, "Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition."* Compounds were tested at a worst-case concentration – at least three-fold greater than therapeutics concentrations. Samples from 11 different donors were assayed in singlicate across eight VerifyNow PRUTest instruments with one device lot of VerifyNow PRUTest using a randomized scheme. Interference testing was performed with six donors using native blood samples and blood samples spiked with 2-MeSAMP, a P2Y12 receptor inhibitor.

Table K. Interfering Substance

		2-MeSAMP not added			2-MeSAMP added		
Interferent / Test concentration		**Mean PRU Control**	**Mean PRU Test**	**Pct. Recovery**	**Mean PRU Control**	**Mean PRU Test**	**Pct. Recovery**
A3P5PS[a]	100 µM	274.3	265.0	96.6	96.8	97.0	100.3
Acetaminophen	1.32 mM	274.3	263.7	96.2	96.8	99.1	102.5
Betamethasone	64 µM	274.3	270.5	98.6	96.8	95.1	98.3
Caffeine	306 µM	274.3	264.8	96.5	96.8	99.5	102.8

Captopril	23 µM	274.3	262.9	95.9	96.8	100.0	103.4
Catechin	86 µM	274.3	273.1	99.6	96.8	99.0	102.3
Celecoxib	8.5 µg/mL	318.3	319.1	98.0	129.9	128.0	98.6
Cilostazol	60 µM	328.8	326.6	99.4	139.6	141.8	101.5
Cimetidine	79 µM	328.8	315.3	95.9	139.6	140.9	100.9
DMSO[b]	0.11%	318.3	322.1	98.9	129.9	131.9	101.5
Dipyridamole	20 µM	328.8	319.9	97.3	139.6	146.8	105.1
Diltiazem	15 µM	328.8	321.1	97.7	139.6	139.9	100.2
Ethanol	87 mM	328.8	321.1	97.3	139.6	141.5	101.3
Fish oil	32 mg/mL	328.8	317.1	96.5	139.6	142.0	101.7
Glucosamine HCl	9.4 µM	201.4	205.8	102.2	139.4	137.2	98.4
Heparin, LMW[c]	1833 U/L	201.4	208.6	103.6	139.4	141.8	101.7
Hydrochlorothiazide	20 µM	201.4	204.3	101.4	139.4	138.5	99.4
Ibuprofen	2.4 mM	201.4	200.0	99.3	139.4	137.4	98.6
Insulin	3 ng/mL	201.4	208.9	103.7	139.4	134.9	96.8
Lidocaine	51 µM	201.4	206.8	102.7	139.4	137.5	99.6
Nitroglycerin	0.1 µg/mL	249.5	241.0	96.6	129.8	132.1	101.8
Norfluoxitine	7.27 µM	249.5	241.4	96.7	129.8	132.4	102.0
Norverapamil	4.5 µM	249.5	243.3	97.5	129.8	133.8	103.1
Omeprazole	4.5 µM	269.1	265.6	98.8	142.0	143.9	101.3
Oxypurinol	99 µM	249.5	242.0	97.0	129.8	131.3	101.2
Pravastatin	56 µM	249.5	249.1	99.9	129.8	129.9	100.1
Propranolol	7.7 µM	249.5	242.8	97.3	129.8	135.6	104.5
Salicylic acid	4.3 mM	249.5	241.1	96.6	129.8	128.9	99.3
Streptokinase	400 U/mL	325.6	317.6	97.5	129.9	132.6	102.1
Theophylline	220 µM	325.6	318.3	97.8	129.9	131.4	101.2
L-Thyroxine	32 nM	201.4	198.5	98.6	139.4	138.4	99.3
α-Tocopherol	58 µM	318.3	311.1	96.5	129.9	133.1	102.5
Triglycerides	37 mM	318.3	315.9	97.0	129.9	129.3	99.5
Warfarin	32 µM	318.3	319.1	98.0	129.9	129.4	99.6

[a] *Putative thiamine-phosphate pyrophosphorylase*
[b] *DMSO = dimethyl sulfoxide c LMW = low molecular weight*

Each interferent spiked into whole blood samples at the above concentrations showed percent recovery which deviated less than 10% from baseline PRUTest values. Therefore, none of these substances significantly interfere with VerifyNow PRUTest results.

Stability

Wet Quality Controls (WQC)

Device stability of the VerifyNow PRUTest reagent device has been evaluated over nine months. Three lots of WQC level 1, three lots of WQC Level 2 and three lots of reagent devices are stored at -70°C and at 20±5 °C. Each of the three lots of WQC levels 1 and 2 were tested with the three lots of reagent devices at time zero, 3, 6, and 9 months under both storage conditions.

WQC Level 1

WQC Level 1 simulates a patient sample with highly inhibited platelets and does not produce a significant aggregation profile. The CVs for Level 1 WQC are not calculated because the nominal PRU value is zero. The acceptance criterion for stability of WQC Level 1 was a PRU result < 30. At the nine-month time point, the range of PRU values generated with WQC Level 1 did not exceed 30 PRU.

WQC Level 2

The acceptance criterion for stability for WQC Level 2 was percent recovery ≥ 90 to ≤ 110% of the baseline PRU result. At the nine-month time point, percent recovery of WQC Level 2 passed acceptance criterion for stability when compared to time zero.

Isochronous reagent stability study with donor whole blood samples

Each of three reagent lots was tested at time zero, 3, 6, and 9 months using whole blood samples from normal donors. The acceptance criterion for stability for whole blood samples was percent recovery ≥ 90 to ≤ 110% of the baseline PRU result. At the nine-month time point, percent recovery of PRUTest results in whole blood passed acceptance criterion for stability when compared to time zero. This further supports the nine month stability claim for VerifyNow™ PRUTest reagent storage at 20±5 ºC.

Conclusion

The results of this study indicate that the PRUTest device is stable for up to nine months when stored at ambient temperature (20°C ± 5°C).

Table L. WQC Level 1 Results: 3, 6, and 9 Month Stability

20 ± 5°C Condition							
Time Zero		3 Months		6 Months		9 Months	
N	PRU Range	N	PRU Range	N	PRU Range	N	PRU Range
324	1 -5	108	1 - 3	108	0 - 4	108	0 - 3

At all test intervals, all Level 1 WQC results met the acceptance criteria of ≤30.

Table M. WQC Level 2 Results (Comparison to Control [-70°C]): 3, 6, and 9 months

		3 Months							6 Months							9 Months						
		-70°C Condition			20 ± 5°C Condition				-70°C Condition			20 ± 5°C Condition				-70°C Condition			20 ± 5°C Condition			
		N	Mean	SD	N	Mean	SD	% Difference from -70°C Condition	N	Mean	SD	N	Mean	SD	% Difference from -70°C Condition	N	Mean	SD	N	Mean	SD	% Difference from -70°C Condition
WQC Lot 1	PRUTest Lot 1	6	296	11.6	6	289	6.0	-2.1	6	297	12.1	6	291	8.2	-2.0	6	286	4.9	6	287	13.5	0.3
	PRUTest Lot 2	6	281	9.0	6	276	14.2	-2.0	6	280	17.9	6	288	10.4	3.2	6	285	13.0	6	273	7.2	-4.2
	PRUTest Lot 3	6	271	3.8	6	265	11.8	-2.0	6	265	11.9	6	281	10.3	6.2	6	276	18.0	6	270	13.2	-2.1
WQC Lot 2	PRUTest Lot 1	6	285	7.7	6	293	7.0	2.8	6	287	22.8	6	291	10.3	1.1	6	287	9.2	6	277	9.3	-3.5
	PRUTest Lot 2	6	278	6.5	6	270	7.8	-3.0	6	292	11.6	6	280	8.4	-4.0	6	282	12.0	6	268	11.1	-4.9
	PRUTest Lot 3	6	272	7.9	6	262	7.2	-3.6	6	280	11.8	6	266	10.0	-4.9	6	274	8.6	6	263	11.8	-4.0
WQC Lot 3	PRUTest Lot 1	6	276	11.2	6	288	5.5	4.3	6	291	22.6	6	285	16.1	-2.2	6	295	11.5	6	285	4.6	-3.4
	PRUTest Lot 2	6	271	9.8	6	266	6.9	-1.7	6	292	12.6	6	286	20.6	-2.0	6	278	12.0	6	284	13.4	2.0
	PRUTest Lot 3	6	269	11.9	6	263	9.8	-2.2	6	267	8.7	6	270	23.3	1.4	6	264	4.8	6	272	5.6	3.0
	Aggregated	54	278	11.8	54	275	14.4	-1.1	54	283	18.0	54	282	15.5	-0.5	54	281	13.4	54	275	12.5	-1.9

The table above shows Level 2 WQC Results from the three, six, and nine month time point results using control PRUTest devices stored at ≤ -70 °C compared to those stored at 20 ± 5° C. All lots fell within ± 10% of the control condition (≤ -70 °C)

Table N. Stability at nine-month time point in whole blood compared to -70°C Condition

		9 Months						
		-70 C Condition			20 ± 5°C Condition			
		N	PRU Mean	SD	N	PRU Mean	SD	% Difference From -70 C Condition
Donor 1	PRUTest Lot 1	3	254	12.1	3	235	23.4	-7.6
	PRUTest Lot 2	3	262	14.6	3	239	22.0	-8.9
	PRUTest Lot 3	3	256	4.2	3	274	65.0	7.2
	Aggregated	9	257	10.4	9	249	40.8	-3.2
Donor 2	PRUTest Lot 1	3	184	5.8	3	195	6.9	6.2
	PRUTest Lot 2	3	196	9.9	3	193	4.2	-1.5
	PRUTest Lot 3	3	184	10.0	3	213	45.7	15.7
	Aggregated	9	188	9.6	9	200	25.2	6.6

Whole blood PRU results are shown above Table . Donors were tested at the nine month time point with PRUTest devices stored at 20 ± 5°C and compared to devices stored at ≤ -70°C. For all three PRUTest device lots and both donors the aggregated lot data at (20 ± 5°C) fell within ± 10% of the control condition (≤ -70 °C).

Table O. Stability at nine-month time point in whole blood inhibited with 2-MeSAMP compared to newly manufactured devices

		Recently Manufactured Lot			20 ± 5°C Condition				
		N	PRU Mean	SD		N	PRU Mean	SD	% Difference From Recently Manufactured Lot
Donor 399	Recently Manufactured Lot (Control)	5	140	13.8		5	140	11.9	-0.4
						5	125	13.0	-10.7
						5	136	9.0	-2.7
					Aggregated	15	134	12.4	-4.6
Donor 1077	Recently Manufactured Lot (Control)	5	130	20.3		5	140	10.3	7.4
						5	130	27.3	0.3
						5	144	16.8	2.4
					Aggregated	15	138	18.9	6.1

Inhibited whole blood PRU results are shown above Table. Donors were tested at the nine month time point with PRUTest devices stored at 20 ± 5°C and compared to newly manufactured devices. For all three PRUTest device lots and both donors the aggregated lot data at (20 ± 5°C) fell within ± 10% of the control condition.

Conclusions drawn from the nonclinical and clinical performance studies:

The results of the bench and clinical performance testing demonstrate that the VerifyNow PRUTest (subject device) is substantially equivalent in performance to the predicate VerifyNow P2Y12 Assay (predicate device).